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NATURAL COMPOUNDS
IN CANCER PREVENTION AND TREATMENT

BOOK OF ABSTRACTS



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ENGINEERING BENZYLGLUCOSINOLATE INTO TOBACCO

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The link between regular consumption of cruciferous vegetables and a reduced risk of developing cancer is well established. This cancer-preventive activity has been attributed to glucosinolates, which are defence compounds characteristic of cruciferous plants. We report engineering the production of the bioactive benzylglucosinolate in the non-cruciferous plant *Nicotiana benthamiana*. The study includes identification of a biosynthetic enzyme, γ -glutamyl peptidase 1 (GGP1), which substantially increases benzylglucosinolate production. GGP1 was shown to metabolize a glutathione conjugate that otherwise accumulates to large extents. Its discovery elucidates an uncharacterized step in the biosynthesis of glucosinolates and expands the reaction repertoire of enzymes containing glutamine amidotransferase domains. The ability to engineer benzylglucosinolate provides the basis for heterologous production of glucosinolates aimed at utilization in cancer-prevention. The engineering strategy developed has great potential as a generally applicable technological platform for gene discovery and proof-of-concept engineering of complex biosynthetic pathways leading to valuable phytochemicals.

BIOTECHNOLOGICAL ALTERNATIVE IN PRODUCTION OF BIOACTIVE SUBSTANCES IN THE GENUS HYPERICUM

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Medicinal plants from the genus *Hypericum*, especially *H. perforatum* that is the most studied one from about 450 species, are attracting considerable interest for centuries. Modern pharmacological studies demonstrate high efficacy of some metabolites, namely naphthodianthrones and acylphloroglucinols with a wide range of activities and sometimes with insufficiently defined pharmaceutical function. Knowledge on biosynthesis of bioactive substances in the representatives of the genus *Hypericum* and genes encoding for key enzymes in their biosynthetic pathways is very limited. This all suggests for further detail biological and genetic studies of the genus/species. The inconsistent chemical profiles are a result of genetics related to secondary metabolite biosynthesis, physiology and plant-environmental interactions.

In early nineties of the last century when new activities of a dianthrone hypericin, such as anticancer and antiviral have been reported, *H. perforatum* L. as a natural source of hypericin has developed into a model species for biotechnological and genetic studies in our laboratory.

The biotechnological approach in study/production of desirable secondary metabolites by the representatives of the genus *Hypericum* comprises:

- i) development of an effective regeneration system in vitro by either direct organogenesis or somatic embryogenesis for high-producing genotypes/species;
- ii) widening of genetic variation via indirect regeneration from callus;
- iii) development of an effective transformation system for studying the gene function and/or for production purposes;
- iv) studying the candidate genes in biosynthesis of bioactive compounds and affecting their expression;
- v) design of small-scale cultivation of explants in bioreactor under controlled conditions;
- vi) development of an effective cryopreservation protocols for establishment of gene bank.

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